PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 0313487262	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416).
International Application No. **PCT/AU2003/001209**	International Filing Date *(day/month/year)* 16 September 2003	Priority Date *(day/month/year)* 16 September 2002
International Patent Classification (IPC) or national classification and IPC **Int. Cl.** [7] C07K 16/30; A61K 39/395; A61P 35/00		
Applicant THE QUEEN ELIZABETH HOSPITAL RESEARCH FOUNDATION INC. et al		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheet(s).

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand 7 April 2004	Date of completion of the report 10 January 2005
Name and mailing address of the IPEA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	Authorized Officer **CHRISTINE BREMERS** Telephone No. (02) 6283 2313

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/AU2003/001209

I. Basis of the report

1. With regard to the elements of the international application:*

[X] the international application as originally filed.

[ ] the description, pages , as originally filed,
pages , filed with the demand,
pages , received on with the letter of

[ ] the claims, pages , as originally filed,
pages , as amended (together with any statement) under Article 19,
pages , filed with the demand,
pages , received on with the letter of

[ ] the drawings, pages , as originally filed,
pages , filed with the demand,
pages , received on with the letter of

[ ] the sequence listing part of the description:
pages , as originally filed
pages , filed with the demand
pages , received on with the letter of

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language which is:

[ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

[ ] the language of publication of the international application (under Rule 48.3(b)).

[ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

[ ] contained in the international application in written form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readable form.

[ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

4. [ ] The amendments have resulted in the cancellation of:

[ ] the description, pages

[ ] the claims, Nos.

[ ] the drawings, sheets/fig.

5. [ ] This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report*

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims **1-29**	**YES**
	Claims	**NO**
Inventive step (IS)	Claims	**YES**
	Claims **1-29**	**NO**
Industrial applicability (IA)	Claims **1-29**	**YES**
	Claims	**NO**

2. Citations and explanations (Rule 70.7)

Novelty and Inventive Step

D1 BENNETT B. D. *et al.*, Journal of Biological Chemistry (1994), vol. 269, no. 19, pages 14211-14218

D2 TAKAI N. *et al.*, , Oncology Reports (2001), vol. 8, no. 3, pages 567-573

D3 STEPHENSON S.-A. *et al.*, BMC Molecular Biology (2001), vol. 2, no. 1, article 15, pages 1-9

D4 HALL S. M. *et al.*, American Journal of Respiratory Cell and Molecular Biology (2002), vol. 26, no. 3, pages 333-340

D5 WO 2002/26827 A1 (NOVARTIS AG), 4 April 2002

D6 LIU W. *et al.*, "Coexpression of Ephrin-Bs and their Receptors in Colon Carcinoma", Cancer (2002), vol. 94, no. 4, pages 934-939

D1-D6 were cited in the ISR.

D1 discloses EphB4 (then known as HTK) as a receptor protein, its sequence, its presence in various tissues and an antibody to its extracellular domain (ecd). See the abstract and page 14217 column 2. Also disclosed is that EphB4 may be implicated in malignant transformation (see page 14211 column 1- column 2 paragraph 2).

D2 discloses ecd antibodies for EphB4 and a role for EphB4 in endometrial carcinoma and tumour progression and estrogen dependent proliferation, and its use as a diagnostic and prognostic marker and target for therapies (see page 572 column 2 conclusion).

Each of D1 and D2 show that EphB4, its ecd antibodies and its role in cancer are known. When a role is found for a known protein then it is known to use antibodies to inhibit that role. It is then a matter of experimentation to find the epitope for the antibody that inhibits that role. Therefore, there is no inventive step in determining the epitope location. Therefore claims 1-29 are not inventive.

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

1. Claim 29 is not fully supported by the specification because the claim is to an agent per se, the essential features of which have not been fully defined. Its structure or sequence cannot be fully determined and may include known compounds.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of Box V

D3 discloses EphB4 gene and receptor protein as a candidate tumour-specific gene marker for colon cancer and the use of EphB4-specific antibodies for immunohistochemical analysis. D3 may be combined with D1 or D2. Therefore claims 1-29 are not inventive.

D6 discloses EphB4 mRNA expression in colon carcinomas and use of primary antibodies directed against EphB4 for immunohistochemical analysis. D6 may be combined with D1 or D2. Therefore claims 1-29 are not inventive.

D4 discloses EphB4 antibodies.
D5 discloses an isolated soluble polypeptide comprising an amino acid sequence of an extracellular region of an Eph receptor.
D4-D5 are cited to show the general state of the art.